**Table 1. Health Effect Levels of Malathion in Humans and Laboratory Animals (continued)**

| Route | Duration | Species | NOAEL | LOAEL | Organ/Effect | Comments | Reference |
|---|---|---|---|---|---|---|---|
| oral | once | rat | | 200–12,500 mg/kg | $LD_{50}$ range | Reported $LD_{50}$ values depend on the purity of the compound, with technical-grade malathion being more toxic than the pure compound. Young animals are more susceptible than older animals. | Hazelton and Holland 1953; Aldridge et al. 1979; NIOSH 1976; IARC 1983; HSDB 2002; Lu et al. 1965; Gaines 1969; Mendoza 1976; Umetsu et al. 1977. |
| oral | once | mouse | | 1,000–4,059 mg/kg | $LD_{50}$ range | Reported $LD_{50}$ values depend on the purity of the compound, with technical-grade malathion being more toxic than the pure compound. | Hassan and Dauterman 1968; Hazleton and Holland 1953; IARC 1983.; Rodgers et al 1986; Talcott et al. 1979; Umetsu et al. 1977 |
| oral | once | rabbit | | 1,200 mg/kg | Death | Five of six rabbits died 6 hours after dosing. | Weeks et al. 1977 |
| oral | once | rat | | 500 mg/kg | Increased activities of liver enzymes in serum indicative of liver toxicity | Technical-grade malathion (96%) | Enan 1983 |
| oral | once | rat | | 4.4 mg/kg | Decreased hematocrit and platelet counts | Malathion 99% | Lox 1983 |
| oral (corn oil) | once | rat | 1,000 mg/kg | 2,000 mg/kg | Neurotoxicity—decreased motor activity and clinical signs; decreased plasma and erythrocyte cholinesterase activity | No inhibition of brain cholinesterase at any dose. Technical-grade malathion (96.4%) | Lamb 1994a |
| oral | once | rat | | 1,950 mg/kg | Hemorrhage and hyperemia in the lungs; congestion and hemorrhage in the heart; liver necrosis, congestion and hemorrhage; kidney congestion, degenerative changes in tubular epithelium | Technical-grade malathion (95%) | Piramanayagam et al. 1996 |

**Table 1. Health Effect Levels of Malathion in Humans and Laboratory Animals (continued)**

| Route | Duration | Species | NOAEL | LOAEL | Organ/Effect | Comments | Reference |
|---|---|---|---|---|---|---|---|
| oral | once | rat | | 600 mg/kg | Increased spontaneous motor activity; dose-related increase in inhibition of cholinesterase and neurotoxic esterase in brain and spinal cord | At the highest dose of 2,000 mg/kg, brain and spinal cord cholinesterase activities were inhibited by 56% and 47%, respectively. | Ehrich et al. 1993 |
| oral | 7 days | rat | 163 mg/kg/day | 411 mg/kg/day | Dizziness, recurrent convulsions, tremors; severe respiratory distress | The effects were more serious at the highest dose of 593 mg/kg/day, and tachycardia occurred at the highest dose. | Ojha et al. 1992 |
| oral | 8 days (gestation days 6–13) | rat | 138 mg/kg/day | 276 mg/kg/day | 34% Inhibition of brain cholinesterase | Convulsions, tremor, and ataxia occurred at the high dose of 827 mg/kg/day. Also at 827 mg/kg/day, 47% inhibition of brain cholinesterase occurred in the pups. | Matthews and Devi 1994 |
| oral (gavage) | 3 day | rat | | 500 mg/kg/day | Dyspnea; decreased glutathione content and increased lipid peroxide in liver and kidney | Pregnant rats were treated on gestational days 6, 10, and 14. | Prabhakaran et al. 1993 |
| oral (gavage) | 6 days | rat | | 225 mg/kg/day | increased pituitary gland weight and serum prolactin levels, decrease in pituitary prolactin | Purity not specified. | Simionescu et al. 1977 |
| oral (drinking water) | 14 days | rat | | 89 mg/kg/day | Changes in clotting factors | At low dose, increase in fibrinogen and decrease in clotting factor XII; at 111 mg/kg/day, decrease in clotting factor II and XII and increase in factor X. | Lox 1985 |
| oral | once | mouse | | 720 mg/kg | Tremors, fasciculation, 36% inhibition of brain cholinesterase; suppression of primary IgM response | The experimental result suggested that cholinergic stimulation plays a role in the organophosphate-induced suppression of the splenic antibody-forming cell. Erythrocyte and plasma cholinesterase were inhibited by 47% and 59% at 240 mg/kg. | Casale et al. 1983 |

**Table 1. Health Effect Levels of Malathion in Humans and Laboratory Animals (continued)**

| Route | Duration | Species | NOAEL | LOAEL | Organ/Effect | Comments | Reference |
|---|---|---|---|---|---|---|---|
| oral | once | mouse | | 715 mg/kg | Increased proliferative response of splenoncytes after exposure to metabolic activators | Metabolic activation was necessary for this response. | Rodgers and Ellefson 1990 |
| oral | once | mouse | | 450 mg/kg | Stimulation of macrophage function | Mediators from cells may contribute to the increase in macrophage function. | Rodgers and Xiong 1996a |
| oral | once | mouse | 1 mg/kg | 10 mg/kg | Increased serum histamine levels | The consequences of the mast cell degranulation that results from malathion administration is not localized and symptoms such as lacrimation, rashes, and irritation of mucous membranes resulting from aerial malathion spraying may be systemic. | Rodgers and Xiong 1997b |
| oral (gavage) | 14 days | mouse | | 0.1 mg/kg/day | Degranulation of mast cells associated with the small intestine | Malathion elevated macrophage function and led to mast cell degranulation in all tissues examined. | Rodgers and Xiong 1997c |
| oral | once | rabbit | | 188 mg/kg | 50%–60% Inhibition of brain cholinesterase | Inhibition was observed in four brain areas—cerebral right frontal lobe, cerebral left frontal lobe, cerebellum lateralis, and cerebellum flocculus. | Vijayakumar and Selvarajan 1990 |
| oral | once | rabbit | 12 mg/kg | 120 mg/kg | 27% Inhibition of erythrocyte cholinesterase | Cholinesterase activity was inhibited by 61% at 600 mg/kg and 79% at 1,200 mg/kg. | Weeks et al. 1977 |
| oral | once | hen | 1,007.5 mg/kg | | Acute delayed neurotoxicity | No signs occurred of delayed neurotoxicity. Technical-grade malathion (93.6%) | Fletcher 1988 |
| inhalation | 5–10 minutes | human | 21 mg/m$^3$ | 85 mg/m$^3$ | Nasal irritation | No other signs of toxicity occurred. | Golz 1959 |
| inhalation | 4 hours | rat | | | $LC_{50}$ | The $LC_{50}$ was >5,200 mg/m$^3$. Technical-grade malathion (96%/98%) | Jackson et al. 1986 |
| inhalation | 6 hours | rabbit | 65 mg/m$^3$ | 123 mg/m$^3$ | 38% Inhibition of erythrocyte cholinesterase | No signs of toxicity or deaths occurred. | Weeks et al. 1977 |

**Table 1. Health Effect Levels of Malathion in Humans and Laboratory Animals (continued)**

| Route | Duration | Species | NOAEL | LOAEL | Organ/Effect | Comments | Reference |
|---|---|---|---|---|---|---|---|
| **Intermediate Duration Toxicity** | | | | | | | |
| dermal | 30 days once/day | guinea pig | | 200 mg/kg/day | Death; 45%–52% inhibition of brain and erythrocyte cholinesterase at 200 and 400 mg/kg/day | Death occurred in 4/10 during days 20–30. Other effects included hyperkeratosis of the skin. | Dikshith et al. 1987 |
| dermal | 3 weeks 6 hr/day 5 d/wk | rabbit | 50 mg/kg/day | 300 mg/kg/day | Inhibition of erythrocyte, plasma, and brain cholinesterase at 300 and 1,000 mg/kg/day | No clinical signs of toxicity; no effects on body weight, food consumption, organ weights, hematologic, clinical chemistry parameters; no dermal reactions; gross and histologic examination unremarkable. Technical-grade malathion (94%) | Moreno 1989 |
| oral (capsule) | 32–56 days once a day | human | 0.23 mg/kg/day | 0.34 mg/kg/day | 25% Depression of plasma and erythrocyte cholinesterase | No clinical signs of toxicity, no effects on blood counts or urinalyses. The malathion (purity not reported) was given in corn oil in a capsule. | Moeller and Rider 1962 |
| oral (diet) | 4–6 weeks | rat | | 62–68 mg/kg/day | 50% Inhibition of brain, erythrocyte and plasma cholinesterase | No other adverse effects were noted. | NIOSH 1976; IARC 1983 |
| oral (diet) | 8–22 weeks | rat | 2.3 mg/kg/day | 5.8 mg/kg/day | Reduced humoral and cell-mediated immune response to antigens | No effect was seen on serum IgG or IgM levels. | Banerjee et al 1998 |
| oral (diet) | 90 days | rat | 4 mg/kg/day | 352–395 mg/kg/day | Inhibition of brain, erythrocyte and plasma cholinesterase | At higher doses (1,486 and 1,575 mg/kg/day), cholinergic signs of toxicity, greater inhibition of brain cholinesterase, and reduced body weight gain were observed. Technical-grade malathion (96.4%) | Lamb 1994b |
| oral (diet) | 90 days | rat | 38 mg/kg/day | 75 mg/kg/day | Increased excitability as shown by changes in electroencephalogram and electromyogram | Running time was dose-dependent and indicated increased nervous excitability. Cholinesterase in the cerebral cortex was inhibited by 18% in rats sacrificed after 21 days. | Desi et al. 1978 |

**Table 1. Health Effect Levels of Malathion in Humans and Laboratory Animals (continued)**

| Route | Duration | Species | NOAEL | LOAEL | Organ/Effect | Comments | Reference |
|---|---|---|---|---|---|---|---|
| oral (drinking water) | 6 months | rat | | 0.15 mg/kg/day | Prolonged prothrombin and partial thromboplastin times; hepatocyte degeneration | No effect was observed on fibrinogen, coagulation factors II, V, VII, or X, or on hematocrit or platelet counts | Lox and Davis 1983 |
| oral (diet) | 3–12 weeks | mouse | 4.2 mg/kg/day | 10.5 mg/kg/day | Decreased humoral and cell-mediated response to antigens | No effect was observed on serum IgG or IgM levels | Banerjee et al.1998. |
| oral (gavage) | 90 days | mouse | | 0.1 mg/kg/day | Increased macrophage function and mast cell degranulation | Malathion administration elevated some macrophage functions and led to mast cell degranulation in all tissues examined. | Rodgers and Xiong 1997d |
| oral (gavage) | 15 weeks | rat | | 10 mg/kg/day | Significant decrease in serum cortisol and aldosterone levels, and congestion in zona reticularis of adrenal glands | No effects were observed on T3, T4, testosterone, estradiol 17-β levels. | Ozmen and Akay 1993 |
| oral (gavage) | 21 weeks | rabbit | 0.5 mg/kg/day | 2.5 mg/kg/day | Decrease in humoral and cell-mediated immunity | No effect was observed on serum IgG or IgM levels | Banerjee et al. 1998 |
| oral (capsule) | 6 weeks, 5 days/week | rabbit | 10 mg/kg/day | 25 mg/kg/day | 25%–30% Inhibition of erythrocyte cholinesterase | The purity of malathion was not specified, and little detail was presented. | Desi et al. 1978 |
| oral (capsule) | 6 weeks, 5 days/week | rabbit | | 5 mg/kg/day | Decreased humoral immune response to *Salmonella* vaccine | The purity of malathion was not specified, and little detail was presented. | Desi et al. 1978 |
| oral (capsule) | 28 days | dog | | 125 mg/kg/day | Inhibition of plasma and erythrocyte cholinesterase | The dogs treated with malathion at ≥120 mg/kg/day had diarrhea. | Fischer et al. 1988 |
| oral (capsule) | 1 year | dog | | 62.5 mg/kg/day | Inhibition of plasma and erythrocyte cholinesterase | No deaths and no clinical signs of toxicity occurred at doses up to 250 mg/kg/day. Technical-grade malathion (95%) | Tegeris Laboratories, Inc. 1987 |
| inhalation | 42 days | human | 21 mg/m$^3$ | 85 mg/m$^3$ | Nasal and eye irritation | Irritation occurred during the first 5–10 minutes of each exposure. No effects were observed on erythrocyte or plasma cholinesterase activity. | Golz 1959 |

**Table 1. Health Effect Levels of Malathion in Humans and Laboratory Animals (continued)**

| Route | Duration | Species | NOAEL | LOAEL | Organ/Effect | Comments | Reference |
|---|---|---|---|---|---|---|---|
| inhalation. | 13 weeks<br>6 hrs/day<br>5 days/wk | rat | | 100 mg/m$^3$ | Inhibition of plasma and erythrocyte cholinesterase; slight to moderate lesions in nasal cavity and larynx | Clinical signs (urogenital staining, excessive salivation, ungroomed fur) occurred mainly at the highest level (2,010 mg/m$^3$) but also at 100 and 450 mg/m$^3$. | Beattie 1994 |
| **Chronic Duration Toxicity** | | | | | | | |
| oral (diet) | 2 years | rat | 2.4 mg/kg/day | 29–35 mg/kg/day | Inhibition of erythrocyte and plasma cholinesterase | Increased mortality in males occurred at 359 mg/kg/day and higher. At higher doses, other effects included decreased body weight gain, effects on hematologic and clinical chemistry parameters, and organ weights. Histopathologic effects included lesions in the nasal mucosa and nasal pharynx and chronic nephropathy. At the highest dose (868 mg/kg/day), incidence of combined hepatocellular adenoma and carcinoma increased in female rats. | Daly 1996a |
| oral (diet) | 2 years | rat | | 166 mg/kg/day | Chronic inflammation of the stomach and stomach ulcers; fatty metamorphosis of the liver | No clear evidence was found of an association of tumor incidence with administration of malathion. | NCI 1979 |
| oral (diet) | 80 weeks | mouse | | 2980 mg/kg/day | Coughing and sneezing from week 72 until end of study; generalized body tremor from weeks 71–79 | No histologic evidence was found of treatment-related non-neoplastic or neoplastic lesions. | NCI 1978 |

**Table 1. Health Effect Levels of Malathion in Humans and Laboratory Animals (continued)**

| Route | Duration | Species | NOAEL | LOAEL | Organ/Effect | Comments | Reference |
|---|---|---|---|---|---|---|---|
| oral (diet) | 18 months | mouse | 17.4–20.8 mg/kg/day | 143–167 mg/kg/day | Inhibition of plasma and erythrocyte cholinesterase; increased incidence of non-neoplastic nasal lesions | At higher doses (≥1,476 mg/kg/day), effects included decreased body weight and food consumption, increased liver weight, and increased incidence of hepatocellular hypertrophy. Brain cholinesterase was inhibited at 2,978–3,448 mg/kg/day. At 1,476 and 2,978 mg/kg/day, male mice had increased incidence of combined hepatocellular carcinoma and adenoma. | Slauter 1994 |
| **Developmental/Reproductive Toxicity** | | | | | | | |
| oral (gavage) | 2 days | rat | | 40 mg/kg/day | Reversible damage of spermatogenic tissue | The damage included a reduced number of Sertoli and Leydig cells, reduced A-spermatogonia, and reduced pachytene spermatocytes. | Krause et al. 1976 |
| oral (gavage) | 20 days | rat | | 20 mg/kg/day | Reversible damage of spermatogenic tissue | The damage included reduced numbers of Sertoli cell, A-spermatogonia and pachytene spermatocytes. | Krause et al. 1976 |
| oral | 3 days, gestation days 28–30 | rabbit | | 126 mg/kg/day | 79% Decrease in fetal plasma cholinesterase, 66% decrease in fetal brain cholinesterase | The results show that malathion and/or metabolites cross the placenta. | Machin and McBride 1989 |
| oral (gavage) | 3 day | rat | | 500 mg/kg/day | Fewer implants per dam; reduced number of live fetuses per litter and fetal weight | Pregnant rats were treated on gestational days 6, 10, and 14. | Prabhakaran et al. 1993 |
| oral (diet) | 7 days | rat | 18.5 mg/kg/day | 163 mg/kg/day | Minor histopathologic lesion in testes, ovaries, and uterus | Similar effects with more severity occurred at higher doses. | Ojha et al. 1992 |
| oral (gavage) | gestation days 6–15 | rat | 800 mg/kg/day | | No indication of developmental toxicity in offspring | Maternal toxicity (urine staining, decreased body weight and food consumption) at 800 mg/kg/day, but not at 400 mg/kg/day. Malathion 94% | Lochry 1989 |

**Table 1. Health Effect Levels of Malathion in Humans and Laboratory Animals (continued)**

| Route | Duration | Species | NOAEL | LOAEL | Organ/Effect | Comments | Reference |
|---|---|---|---|---|---|---|---|
| oral (gavage) | gestation days 6–18 | rabbit | 25 mg/kg/day | 50 mg/kg/day | Increased mean resorption sites | Maternal toxicity (anorexia, soft stools) at 100 mg/kg/day, decreased body weight gain at 50 mg/kg/day. Malathion 92.4%. No effects observed on fertility, number of corpora lutea, or implantation sites. | Siglin 1985a |
| oral (gavage) | gestation days 6–18 | rabbit | 400 mg/kg/day | | No gross abnormalities | Maternal toxicity at 200 and 400 mg/kg/day: increased mortality, tremors, reduced activity, increased salivation. Maternal NOAEL 100 mg/kg/day. Malathion 92.4% | Siglin 1985b |
| oral (gavage) | 14 days | rat | | 10 mg/kg/day | Significant increase in serum FSH levels | No significant changes in serum LH and testosterone, testis and seminal vesicles weight; spermatogenic epithelium was normal. | Krause 1977 |
| oral (gavage) | 12 weeks | rats | | 44–45 mg/kg/day | Edema, congestion, and desquamation of lining cell of seminiferous tubules; decreased seminal vesicle pH, protein content, relative testes weight, and enzyme activities | Malathion was 90% pure. | Balasubramanian et al. 1987a, 1987b |
| oral (diet) | 2 generations | rat | 131–153 mg/kg/day | 394–451 mg/kg/day | Decreased pup body weights in F1 and F2 pups during late lactation | Parental NOAELs were 394–451 mg/kg/day, and LOAELs were 612–703 mg/kg/day on the basis of decreased body weights during gestation and lactation and decreased F1 premating body weights. | Schroeder 1990 |
| oral (gavage) | 15 weeks | rat | | 10 mg/kg/day | Hyperemia of the veins of the testes and degenerated testicular tubuli | No histopathologic effects on the ovaries were observed | Ozmen and Akay 1993. |